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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/026,066	12/07/2001	John J. L. Simard	40000220-0021-003	8425

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EXAMINER	
VANDERVEGT, FRANCOIS P	
ART UNIT	**PAPER NUMBER**
1644	
MAIL DATE	**DELIVERY MODE**
11/30/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/026,066	SIMARD ET AL.	
	Examiner	Art Unit	
	F. Pierre VanderVegt	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,29-36,38-52 and 54-59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *58 and 59* is/are allowed.

6)☒ Claim(s) *1-5,29-36,38-52 and 55-57* is/are rejected.

7)☒ Claim(s) *54* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 6-28, 37 and 53 have previously been canceled.

Claims 29-36, 58 and 59 have previously been added.

Claims 1-5 29-36, 38-52 and 54-59 are currently pending.

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 31, 2007 has been entered.

In view of Applicant's response filed October 31, 2007 the following grounds of rejection are maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. Claims 1-5, 29, 30, 33-35 and 38-52 and 55-57 stand rejected under 35 U.S.C. 102(b) as being anticipated by Zajac et al (145 on form PTO-1449; Int. J. Cancer [1997] 71:491-496, of record).

It was previously stated: "Zajac teaches isolated T cells that recognize the HLA-A2.1-restricted housekeeping epitope consisting of amino acid residues 27-35 of the MelanA tumor-associated antigen from melanoma target cells (Abstract and page 491, first column in particular)[claims 1, 3, 29, 30, 33-35]. Zajac teaches that tumor-infiltrating-lymphocytes (TILs) were isolated from melanoma patients were able to specifically lyse target cells (pages 492-493 and Figure 2 in particular). The TILs qualify as being "isolated from an immunized animal" because they were obtained from melanoma patients and were therefore "immunized" to the antigen by the presence of the tumor in their body [claim 5]. Accordingly, prior to transformation of the cell line the reactive T cells were present in human serum, a carrier suitable for administration to a human. The composition satisfies the metes and bounds of the claims. Zajac further teaches specific lysis of the target cells by the HLA-A2.1 restricted T cell lines HBL and D10 (Figures 2 and 3 in particular), showing that the composition isolated from the human subject comprised

at least a first and a second T cell population that were directed to epitopes which were not the same [claim 42]. The prior art teaching clearly anticipates the claimed invention.

Claims 40, 41, 56 and 57 are included because a blood sample obtained from a human subject would easily have comprised between 10^5 and 10^{11} T cells in total.

Applicant's arguments filed March 5, 2007 have been fully considered but they are not persuasive.

Applicant argues that the teachings of Zajac et al do not anticipate the claimed invention because the T cells of Zajac did not exhibit tumoricidal activity prior to transformation. However, the claim is drawn to a composition suitable for administration to a human comprising "a first isolated T cell" with the desired properties. The claimed composition reads upon a single T cell with the desired housekeeping epitope-binding properties in a suitable carrier. It is well known in the art that the transformation and in vitro stimulation did not give any of the T cells of Zajac the ability to bind to the housekeeping epitope. Any T cell resulting from the in vitro amplification/transformation events was the progeny of a T cell that already had the ability to bind the housekeeping epitope when it was isolated from the donor subject. The fact that no tumoricidal activity was detected before the in vitro amplification/transformation events is simply an indicator that the T cells with the desired binding/tumoricidal properties were present in the donor blood sample in numbers that were too low to produce a detectable response, however, at least one T cell with the desired binding properties was present in the pre-amplification/transformation sample, otherwise there would be no reactivity after the in vitro amplification/transformation events.

Furthermore, Zajac had no need to "disclose or mention" that the T cell that gave rise to the amplified population was suitable for administration to a human because, while the composition must indeed be suitable therefore, "administration to a human" is an intended use that does not change the nature of the composition itself. Irrespective of Applicant's intended use, the artisan can use a housekeeping epitope-reactive T cell in a carrier of human serum in any way that the artisan sees fit, including the in vitro amplification/transformation reactions taught by Zajac.

Applicant's arguments filed October 31, 2007 have been fully considered but they are not persuasive.

Claim 1 has been amended to recite "a sufficient number of a first isolated T cell to be suitable for adoptive administration to a human." Applicant argues that the teachings of Zajac cannot be considered anticipatory because the number of isolated cells in the sample described by Zajac is too low for adoptive administration. This argument is not persuasive because the claim fails to set forth any type of numerical or functional limitation in regard to what would be considered a "sufficient" number of cells. while the number of cells in the sample of Zajac may be a low number, there is no reason why such a low number could not be adoptively administered. There is no limitation in the claims regarding any type of therapeutic effect attributable to the administered cells. All that is required is that the cells can be taken up in some manner and administered to a human subject. A low cell number does not prevent this.

2. Claims 1-5, 29, 30, 33, 34, 36 and 38-41 stand rejected under 35 U.S.C. 102(b) as being clearly anticipated by Kittlesen et al (79 on form PTO-1449; J. Immunol. [1998] 160:2099-2106, of record).

It was previously stated: "Kittlesen teaches isolated T cell lines that recognize the HLA-A1-restricted housekeeping epitope consisting of the amino acid sequence KCDICTDEY of the tyrosinase tumor-associated antigen from melanoma target cells (Abstract and page 2100, first column in particular)[claims 1, 29, 30, 33, 34, 36]. Kittlesen teaches that the tyrosine reactive T cells are obtained from melanoma patients whose tumors express tyrosinase (paragraph bridging pages 2100-2101 in particular) and therefore qualify as being "isolated from an immunized animal" because they were obtained from melanoma patients and were therefore "immunized" to the antigen by the presence of the tumor in their body [claim 5]. Accordingly, prior to transformation of the cell line the reactive T cells were present in human serum, a carrier suitable for administration to a human. The composition satisfies the metes and bounds of the claims. Kittlesen further teaches that the T cell lines were enriched in vitro from polyclonal populations [claim 3] obtained from melanoma patients by repeated rounds of stimulation with the peptide (page 2100, first column in particular) [claims 2, 4]. The prior art teaching clearly anticipates the claimed invention.

Claims 40 and 41 are included because a blood sample obtained from a human subject would easily have comprised between 10^5 and 10^{11} T cells in total.

Applicant argues that the teachings of Kittlesen et al do not anticipate the claimed invention because Kittlesen does not disclose isolated T cells in serum, but only discloses T cells present in tumor samples and therefore would not be suitable for administration to a human. This is incorrect, as Kittleson clearly teaches at page 2100, column 1, that "[m]elanoma-reactive CTL from peripheral blood lymphocytes... were generated in vitro by repeated stimulation with autologous tumor cells." Contrary to Applicant's assertion, the sample indeed does consist of cells in human serum and does not constitutively contain tumor cells. Again, the claim is drawn to a composition suitable for administration to a human comprising "a first isolated T cell" with the desired properties. The claimed composition reads upon a single T cell with the desired housekeeping epitope-binding properties in a suitable carrier. It is well known in the art that the in vitro stimulation did not give any of the T cells of Kittlesen the ability to bind to the housekeeping epitope. Any T cell resulting from the in vitro amplification was the progeny of a T cell that already had the ability to bind the housekeeping epitope when it was isolated from the donor subject. At least one T cell with the desired binding properties was present in the pre-amplification sample, otherwise there would be no reactivity after the in vitro amplification events.

Furthermore, Kittlesen had no need to "disclose or mention" that the T cell that gave rise to the amplified population was suitable for administration to a human because, while the composition must indeed be suitable therefore, "administration to a human" is an intended use that does not change the nature of the composition itself. Irrespective of Applicant's intended use, the artisan can use a housekeeping epitope-reactive T cell in a carrier of human serum in any way that the artisan sees fit, including the in vitro amplification/transformation reactions taught by Kittlesen."

Applicant's arguments filed October 31, 2007 have been fully considered but they are not persuasive.

Claim 1 has been amended to recite "a sufficient number of a first isolated T cell to be suitable for adoptive administration to a human." Applicant argues that the teachings of Kittlesen cannot be considered anticipatory because the number of isolated cells in the sample described by Kittlesen is too low for adoptive administration. This argument is not persuasive because the claim fails to set forth any type of numerical or functional limitation in regard to what would be considered a "sufficient" number of cells. while the number of cells in the sample of Kittlesen may be a low number, there is no reason why

such a low number could not be adoptively administered. There is no limitation in the claims regarding any type of therapeutic effect attributable to the administered cells. All that is required is that the cells can be taken up in some manner and administered to a human subject. A low cell number does not prevent this.

3. Claims 1-5, 29-32, 35 and 38-41 stand rejected under 35 U.S.C. 102(b) as being clearly anticipated by Jager et al (75 on form PTO-1449; J. Exp. Med. [1998] 187:265-270, of record).

It was previously stated: "Jager teaches isolated CD4+ T cell lines and an HLA-A2 restricted CTL clonal line that recognize housekeeping epitopes of the NY-ESO-1 cancer-testis tumor-associated antigen (Abstract and page 266, first column in particular)[claims 1-3, 29-32, 35]. Jager teaches that the NY-ESO-1 reactive T cells are obtained from PBL and a needle biopsy from a melanoma patient. Jager teaches that the T cells are obtained from a melanoma patient and therefore qualify as being "isolated from an immunized animal" because they were obtained from a melanoma patient that was therefore "immunized" to the antigen by the presence of the tumor in the body [claim 5].

Accordingly, prior to transformation of the cell line the reactive T cells were present in human serum, a carrier suitable for administration to a human. The composition satisfies the metes and bounds of the claims. The prior art teaching clearly anticipates the claimed invention. Claims 40 and 41 are included because a blood sample obtained from a human subject would easily have comprised between 10^5 and 10^{11} T cells in total.

Applicant argues that the teachings of Jager et al do not anticipate the claimed invention because the T cells taught by Jager were generated by incubating peripheral blood lymphocytes from a patient with autologous tumor cells in a culture that also contained antibiotics. Applicant asserts that this makes the CTLs generated unsuitable for administration to a human. However, the peripheral blood lymphocytes are obtained in a blood sample, which is a suspension of cells in serum and constitutes a carrier suitable for human administration. Again, the claim is drawn to a composition suitable for administration to a human comprising "a first isolated T cell" with the desired properties. The claimed composition reads upon a single T cell with the desired housekeeping epitope-binding properties in a suitable carrier. It is well known in the art that the in vitro stimulation did not give any of the T cells of Jager the ability to bind to the housekeeping epitope. Any T cell resulting from the in vitro amplification was the progeny of a T cell that already had the ability to bind the housekeeping epitope when it was isolated from the donor subject. At least one T cell with the desired binding properties was present in the pre-amplification sample, otherwise there would be no reactivity after the in vitro amplification events.

Furthermore, Jager had no need to "disclose or mention" that the T cell that gave rise to the amplified population was suitable for administration to a human because, while the composition must indeed be suitable therefore, "administration to a human" is an intended use that does not change the nature of the composition itself. Irrespective of Applicant's intended use, the artisan can use a housekeeping epitope-reactive T cell in a carrier of human serum in any way that the artisan sees fit, including the in vitro amplification/transformation reactions taught by Jager."

Applicant's arguments filed October 31, 2007 have been fully considered but they are not persuasive.

Claim 1 has been amended to recite "a sufficient number of a first isolated T cell to be suitable for adoptive administration to a human." Applicant argues that the teachings of Jager cannot be considered anticipatory because the number of isolated cells in the sample described by Jager is too low for adoptive administration. This argument is not persuasive because the claim fails to set forth any type of numerical or functional limitation in regard to what would be considered a "sufficient" number of cells. while the number of cells in the sample of Jager may be a low number, there is no reason why such a low number could not be adoptively administered. There is no limitation in the claims regarding any type of therapeutic effect attributable to the administered cells. All that is required is that the cells can be taken up in some manner and administered to a human subject. A low cell number does not prevent this.

Conclusion

4. Claims 58 and 59 are allowed.

5. Claim 54 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to F. Pierre VanderVegt whose telephone number is (571) 272-0852. The examiner can normally be reached on M-Th 6:30-4:00 and Alternate Fridays 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

F. Pierre VanderVegt, Ph.D. /PV/
Patent Examiner

November 26, 2007

MAHER M. HADDAD
PRIMARY EXAMINER